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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,298	06/12/2006	Gordon N. Gill	1034123-000169	6198

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
04/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ADIPFDD@bipc.com

Office Action Summary	Application No.	Applicant(s)	
	10/552,298	GILL ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *11-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-10* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 April 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0706;0906*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election, without traverse, of Invention I and SEQ ID NO: 1, Claims 1-10, in their response of March 17, 2008 is acknowledged. The elected invention is drawn to the polynucleotide of SEQ ID NO: 1 as well as vectors and host cells comprising SEQ ID NO: 1 and methods of making the encoded protein. Claims 1-42 are pending. Claims 11-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-10 are hereby examined.

Priority

The priority date granted for the instant invention is April 1, 2004, the filing date of PCT/US04/10218, which disclosed the elected invention. It is noted that provisional application US 60/459,786 fails to disclose SEQ ID NO: 1 or 2.

Oath-Objections

The Oath is objected to because the change of addresses for Patrick Lin and Michele Yeo in the Oath/Declaration received June 12, 2006 are not dated. See M.P.E.P. 605.04(a), which states that, any changes made to the Oath/Declaration should be initialed and dated by the Applicants prior to execution. The Office will not consider whether noninitialed and/or nondated alterations were made before or after signing of the Oath or Declaration but will require a new Oath or Declaration (37 CFR 1.64). This objection may be overcome by filing an Application Data Sheet.

Title

The title is objected to because it is not descriptive of the elected invention, which is a polynucleotide.

Drawings-Objections

Table 1 and Figure 1 are objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Specification-Objections

The specification is objected to for containing hyperlinks. USPTO policy does not permit the USPTO, i.e, via an issued patent, to refer to any commercial sites, since the USPTO exercises no control over the organization, views or accuracy of the information contained on these outside sites. Hyperlinks and other forms of browser-executable code, especially commercial site URLs, are not to be included in a patent application. (MPEP 608.01) The specification should be carefully checked and all URLs removed.

The specification is objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number

in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

The specification is objected to because it fails to define the abbreviation "TFIIF".

Claims-Objections

Claims 1-10 are objected to for reciting non-elected sequences.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claim 1 is indefinite in the recitation of "hybridizes …under stringent conditions" as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions. The hybridization conditions described in paragraph [0066] are only exemplary and do not define the conditions recited in Claim 1. Thus, Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Since, Claims 2-10 are dependent on Claim 1, said claims are also rejected for the reasons described for Claim 1.

Claim 1 is further rejected under 35 U.S.C. 112, second paragraph, for reciting "conservative substitutions" which is not defined in the specification. Although very common in

the art, the term "conservative substitution" is vague and indefinite. For example, is a Gln/Glu substitution or an Asp/Asn substitution conservative? Are Ser/Tyr and Phe/Tyr conservative substitutions? Another situation that is indefinate is the classification of Gly and Ala; are these small polar residues, similar to Ser, Thr, Gln and Asn, or hydrophobic? Is His basic or hydrophobic? Are linear hydrophobic amino acids similar to aromatic hydrophobic amino acids? Is Cys a small polar amino acid or its own category? Is Tyr a polar amino acid or an aromatic amino acid? Lack of consensus on the answers to these questions causes the term "conservative substitution" to be indefinite. The description of "conservative amino acid substitution" in paragraph [0073] is only exemplary and does not define the substitutions recited in Claim 1. Since, Claims 2-10 are dependent on Claim 1, said claims are also rejected for the reasons described for Claim 1.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, and 5-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 1, does not reasonably provide enablement for any variant thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claim 1 is so broad as to encompass any nucleic acid molecule (i) consisting of a sequence having at least 80% identity to SEQ ID NO: 1, (ii) comprising a sequence having at least 80% identity to SEQ ID NO: 1, (iii) encoding a polypeptide comprising SEQ ID NO: 2 having up to 50 amino acid substitutions, or (iv) hybridizes to SEQ ID NO: 1 under indefinite conditions, wherein the nucleic acid molecule encodes a polypeptide with any or no activity. Claims 5 and 6 are so broad as to encompass any nucleic acid molecule that has at least 90% and 95% identity to SEQ ID NO: 1, respectively, wherein the nucleic acid molecule encodes a polypeptide with any or no activity. It is noted that by use of "comprising" language, these claims encompass polynucleotides, wherein the activity is not derived from the sequence homologous to SEQ ID NO: 1.

The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of nucleic acid molecules broadly

encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO: 2 and the nucleotide sequence of SEQ ID NO: 1.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claim 1, which encompasses all nucleic acid molecules (i) consisting of a sequence having at least 80% identity to SEQ ID NO: 1, (ii) comprising a sequence having at least 80% identity to SEQ ID NO: 1, (iii) encoding a polypeptide comprising SEQ ID NO: 2 having up to 50 amino acid substitutions, or (iv) hybridizes to SEQ ID NO: 1 under indefinite conditions, wherein the nucleic acid molecule encodes a polypeptide with any or no activity. The specification does not support the broad

scope of Claims 5 and 6, which encompasses all nucleic acid molecule that has at least 90% and 95% identity to SEQ ID NO: 1, respectively,, wherein the nucleic acid molecule encodes a polypeptide with any or no activity. The specification does not support the broad scope of Claims 1 and 5 because the specification does not establish: (A) the desired activity for all recited nucleic acid molecules, or the encoded polypeptides (B) regions of the protein structure which may be modified without affecting the desired activity; (C) the general tolerance of the desired activity to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 7-10 further recite vectors, host cells and methods of expressing the nucleic acids of Claim 1, Claims 7-10 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid molecules with an enormous number of modifications of the nucleic acid molecule of SEQ ID NO: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The invention of Claims 2 and 7-10 appears to employ novel cDNAs. Since the cDNAs are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed cDNAs' sequences are not fully disclosed. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the cDNAs. It is noted that applicants have deposited the cDNAs but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein. If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Written Description

Claims 1 and 5-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of nucleic acid molecules (i) consisting of a sequence having at least 80% identity to SEQ ID NO: 1, (ii) comprising a sequence having at least 80% identity to SEQ ID NO: 1, (iii) encoding a polypeptide comprising SEQ ID NO: 2 having up to 50 amino acid substitutions, (iv) hybridizes to SEQ ID NO: 1 under indefinite conditions, or (v) having at least 90% or 95% identity to SEQ ID NO: 1. The specification does not contain any disclosure of the function of all said nucleic acid molecules, or the encoded polypeptides. The genus of polynucleotides that comprise these above nucleic acid molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated nucleic acid molecules are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses the function of only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 1 and 5-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of nucleic acid molecules (i)

consisting of a sequence having at least 80% identity to SEQ ID NO: 1, (ii) comprising SEQ ID NO: 2 having at least 80% identity to SEQ ID NO: 1, (iii) encoding a polypeptide comprising a sequence having up to 50 amino acid substitutions, (iv) hybridizes to SEQ ID NO: 1 under indefinite conditions, or (v) having at least 90% or 95% identity to SEQ ID NO: 1 having any or no activity. The specification teaches the structure of only a single representative species of such nucleic acid molecules. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a variant of SEQ ID NO: 1. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 5-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Venter et al, 2002. Venter et al teach a polynucleotide having 98.2% identity with SEQ ID NO: 1 and

encoding a polypeptide having a single amino acid deletion (see enclosed alignment). Therefore, Claims 1 and 5-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Venter et al, 2002.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3 and 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al, 2003 (filing date 09-FEB-1998) in view of Meinnel et al, 1993. Cocks et al teach a polynucleotide comprising SEQ ID NO: 1, except for a codon encoding the N-terminal methionine. Meinnel et al teach what is well-known in the art; that essentially all protein translation begins with an N-terminal methionine. It would have been obvious to a person of ordinary skill in the art to combine the teachings of Cocks et al and Meinnel et al to modify the polynucleotide of Cocks et al to incorporate a codon encoding an N-terminal methionine. Motivation to do so derives from the desire to enhance recombinant production of the encoded protein for use in biochemical analysis and making an antibody. The expectation of success is high, as methods for modifying polynucleotide are well-known in the art. Therefore, Claims 1-3 and 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cocks et al, 2003 in view of Meinnel et al, 1993.

Allowable Subject Matter

Claim 4 is objected to for reciting non-elected subject matter, but would be allowable if rewritten to recite only the elected sequence.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652